

### Remarks

By the present amendment and response, Applicants have amended claims 1, 13, 21, 24, and 27. Claims 2, 4, and 5 were cancelled previously. Accordingly, claims 1, 3, and 6-34 are pending in the present application, with claims 1, 13, 21, 24, and 27 being independent claims.

Remarks addressing the objections and §103(a) and double patenting rejections contained in the Office Action mailed December 22, 2004 are set forth in turn below.

#### I. Claim Rejections Under 35 U.S.C. § 103(a)

All of the pending claims 1, 3, and 6-34 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable for obviousness over various combinations of cited references, including Ericson (Anal. Chem. 2000), Koehler (U.S. 6,814,859 B2), Soga (U.S. 2003/0230524 A1), Shimada (U.S. 4,137,161) and Hu (U.S. 6,623,860).

Applicants respectfully traverse these rejections and request their withdrawal for the reasons provided below.

#### A. Rejections Under 35 U.S.C. § 103(a) Generally

Three requirements must be met for a *prima facie* case of obviousness. First the prior art reference(s) must teach all of the limitations of the claims. M.P.E.P. § 2143.03. Second, there must be a motivation to modify the reference or combine the teachings of multiple references to produce the claimed invention. M.P.E.P. § 2143.01. Third, a reasonable expectation of success is required. M.P.E.P. § 2143.02. In addition, the teaching or suggestion to combine and the expectation of success must both be found

in the prior art and not based on Applicant's disclosure. M.P.E.P. § 2143.

B. Disclosure of Ericson (Anal. Chem. 2000, Vol. 72, pp. 81-87)

Ericson discloses the fabrication and use of microchips and capillary tubes having continuous polymer beds (serving as stationary phase material) for performing chromatography. Ericson, pg. 81, cols. 1-2. (Such beds are referred to elsewhere as monolithic columns.) The disclosed benefits of using a continuous packed bed are: (1) eliminating "wall effects" by anchoring the beds to the wall of surrounding channel; and (2) **eliminating** the use of **porous frits to retain packed beads** of stationary phase material, recognizing that "the difficulty of affixing frits to support the bed [of packed beads] is obvious." Id. Restating the point, Ericson provides that with a "continuous bed ... anchored to the channel wall ... [n]o supporting frit is, therefore, required." Id. at col. 2.

To fabricate microchips, Ericson teaches the use of photolithographic etching to define channels a quartz substrate. Ericson, pg. 82, cols. 1-2. The quartz chip was mounted on a supporting plate of black Plexiglass with a slit for UV detection. Id., pg. 83, col. 1. Two different microchip designs were employed: one having a serpentine column, and the other purportedly having an "h"-shaped column. Id. at pg. 82, Fig. 2 & caption relating to "C" and "D". Following device fabrication, the channel walls were chemically activated with methacrylol groups to facilitate covalent bonding of polymer bed material. Id. at pg. 83, col. 2. Thereafter, various types of continuous polymer beds (i.e., monolithic columns) were prepared directly in the channels of the microchips by polymerizing monomer solutions in situ. Id. at pg 83, col. 2 – pg. 84, col. 1. A poly(ethylene glycol) solution was used in the outlet channel to create a sharper and

more homogenous end of the polymer bed. Id. at pg. 83, col. 2 – pg. 84, col. 1. UV detection may be performed through the slit in the (Plexiglas) supporting plate at a spot close to (downstream) of the polymer bed. Id. at pg. 84, col. 1. Ericson also discloses that detection could also be done directly through the somewhat UV-transmitting continuous bed, but such detection would be far less preferable due to a tenfold reduction in sensitivity. Id.

Ericson fails to mention the desirability of elevating the backpressure within a detection region, let alone any structure capable of accomplishing such a purpose.

C Disclosure of Koehler (US 6,814,859)

Koehler discloses a multi-column microfluidic separation device having a porous frit disposed between multiple separation columns and multiple exit channels. Koehler, Fig. 3C; col. 7, lines 10-46; col. 10, lines 31-55. Koehler expressly defines a frit as “a microporous material **used to retain stationary phase material within a separation column** for performing liquid chromatography.” Id., col. 4, lines 56-59 (emphasis added). To provide its intended functionality, “[t]he average pore size of the frit 26 is smaller than the average size of the particles of the particulate stationary phase material 220 ... [m]ore preferably ... at least one order of magnitude smaller ... .” Id., col. 7, line 67 – col. 8, line 5. The porous frit permits mobile phase solvent (as well as the sample compound being separated) to flow through the system while keeping stationary phase material within the device. Id., col. 7, lines 40-46 & Fig. 3C. As a result, one surface of a frit is in intimate contact with stationary phase material, and a frit defines one end of a packed column. Id., col. 7, lines 40-46 & Fig. 3C. Koehler teaches the use of polymeric materials, stencil layers, and adhesiveless bonding methods to fabricate microfluidic devices. Koehler, col. 5, lines 13-53; col. 6, lines 21-53.

Notably, Koehler makes **no mention** of the use of “detection regions” (whether or not disposed downstream of a separation column), let alone *additional* porous membranes or materials disposed downstream of a fritted column and detection region.

D. Disclosure of Soga (U.S. 2003/0230524 A1)

Soga discloses a chromatographic chip constructed from a pair of transparent plate members, with the lower plate member defining shallow grooves along its the upper surface that serve as channels and with the upper plate member defining through-holes that correspond to certain of the grooves defined in the lower plate member. Soga, ¶¶ 0010, 0038-0043. In the background of the invention, Soga specifically discusses **problems** associated with using *frits* and filling channels with *microparticle separation media*. Soga, ¶¶ 0005, 0007 (emphasis added). To overcome these difficulties, Soga teaches the synthesis of unified **monolithic** porous bodies – namely, silica gel separation media having a microporous structure that is formed and hardened inside two channels 3, 3' - to yield (monolithic) analysis channels 3, 3'. Soga, ¶¶ 0007, 0010, 0039-0040, 0044-0046. Soga makes no mention of the term “porous membrane.” Detection parts or regions 6, 6' are formed inside the analysis channels 3, 3'. Soga, ¶ 0039. Each analysis channel 3, 3' has independent sample introduction channels 2, 2' and independent mobile phase channels 4, 4', 5, 5'. Soga, Fig. 1 & ¶¶ 0039-0040. Upstream of the analysis channels, reservoir grooves R1-R16 contain test samples (odd-numbered reservoirs) and buffer solutions (even-numbered reservoirs). Soga, Fig. 1 & ¶¶ 0042-0043, 0047-0048. Samples and buffers are introduced into the reservoir grooves R1-R16 by microsyringes. As applied voltages cause test samples to flow through preprocessing channels 2, 2', mobile phase is delivered from mobile phase channels 4, 5, 4', 5' and test samples are introduced into the analysis channels 3, 3' for analysis. Soga, ¶¶ 0047-0048.

E. Disclosure of Shimada (U.S. 4,137,161)

Shimada discloses a liquid chromatography system having a single conventional (e.g., tubular and *not* microfluidic) **packed** separation column 30, an optical detecting device 40 (including a sample flow cell 1 and a reference flow cell 2), and a “flow passage resisting member 90” (consisting of a needle valve, a long capillary tube, or a packed tube) disposed downstream of the detecting device 40 and used to elevate the pressure within the sample cell 1. Shimada, col. 2, line 41 – col. 3, line 15. Because of the presence of the resisting member 90, bubble generation within the effluent from the separation column 30 is suppressed. Shimada, col. 3, lines 13-15.

Shimada teaches that the column 30 *is*, and the resisting member 90 *may be*, packed with particulate material. (*Id.*, col. 1, lines 16-19; col. 2, lines 49-50; col. 3, lines 12-13). Contrary to the Examiner’s assertion (Office Action, page 5), a tube packed with particulate does not constitute a “monolithic” column (i.e., a “monolithic packed column” alleged by the Examiner) as understood in the art and described in the present application, which provides that “[a] porous monolithic region [is] composed of a macroporous crosslinked material.” Because the voids in a monolithic column are formed by crosslinking of polymer chains – not by pressing particles into a tube or other boundary – it is simply nonsensical to refer to a monolith as being “packed”.

In the background of the invention, Shimada **teaches away** from the use of **multiple-column** chromatography systems (i.e., that utilize a separation column and a reference column disposed in parallel) because such systems: are subject to measurement errors due to pressure differences; consume twice as much eluent as single column systems; and require complicated structures. Shimada, col. 1, lines 35-54. Instead, Shimada teaches the use of a sample cell and a detection cell disposed in

parallel downstream of a single chromatographic column to provide sample analyses with reduced measurement error. Id., col. 1, line 55 – col. 2, line 6, col. 5, line 64- col. 6, line 10.

F. Disclosure of Hu (U.S. 6,623,860)

Hu discloses multilevel microfluidic structures fabricated from at least two laminae defining channel microstructures along inner surfaces thereof and communicating across a lamina interface. (Hu et al., col. 2, lines 14-34; col. 3, line 66 – col. 4, line 2; col. 18, lines 23-47). Electrically driven separation processes such as capillary electrophoresis (CE) and/or isoelectric focusing (IEF) are performed in devices according to Hu in separation channels filled with appropriate separation media [i.e., gel and ampholyte-containing gel, respectively]. (Hu, col. 2, lines 56-59; col. 6, lines 34-39; col. 11, line 66 – col. 12, line 30; col. 13, line 58 – col. 14, line 11; col. 15, lines 9-15; col. 15, lines 55-58; col. 16, lines 29-42.) Hu fails to *even mention any* of the following terms relating to the present invention and the context of chromatography: “backpressure,” “chromatography,” “column,” “frit,” “stationary phase,” “packed,” and “porous.”

G. Claims 1, 3, 6-12, 21-23, and 27-33 Are Patentable Over Ericson and Koehler

Claims 1, 3, 6-12, 21-23, and 27-33 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Ericson in view of Koehler (Office Action, pg. 3.) Applicants respectfully traverse these rejections.

1. There Exists No Motivation To Combine Ericson and Koehler To Yield The Combinations of Claims 1, 3, 6-12, 21-23, and 27-33

MPEP § 2143.01 requires the existence of a motivation to modify the reference or combine the teachings of multiple references to produce the claimed invention. Any teaching or suggestion to combine references must be found in the prior art. MPEP § 2143. Contrary to the Examiner's assertion (Office Action, pg. 3), it would **not** have been obvious to combine Ericson and Koehler to arrive at any of claims 1, 3, 6-12, 21-23, and 27-33. Ericson discloses the use of a continuous polymer bed in a microchip or capillary to specifically **avoid** the use of a supporting frit to retain a bed of packed beads. Ericson, col. 2. In sharp contrast to Ericson, Koehler is directed to the fabrication of multi-column chromatography devices specifically **having** a porous retaining frit disposed between particulate-containing separation columns and exit channels. Koehler, Fig. 3C; col. 7, lines 10-46; col. 10, lines 31-55. While Ericson does disclose the use of a detection region, Koehler does not. Neither Ericson nor Koehler mention the desirability of elevating the backpressure within a detection region – let alone any structure capable of accomplishing such a purpose. Since neither reference discloses the desirability for making the claimed combination, and Ericson specifically **teaches away** from the central disclosure of Koehler (incorporating porous frits into devices to retain particulate stationary phase material), one skilled in the art would **not** look to combine the two references to arrive at the claimed combinations. Under these facts, the Examiner has made an impermissible combination of the two references. See MPEP 2145(X)(D)(2) (“[i]t is improper to combine references where the references teach away from their combination”) (*citing In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983)). As a result, with Ericson and Koehler lacking any teaching or suggestion to combine references to produce the claimed invention, there can be no

*prima facie* case of obviousness pursuant to MPEP § 2143.01, and it is respectfully requested that the § 103(a) rejections based on Ericson and Koehler be withdrawn.

2. Ericson And Koehler Fail To Teach All Of The Limitations Of Claims 1, 3 and 6-12

Even if there existed motivation to combine Ericson and Koehler (which there does not), independent claim 1 requires, *inter alia*, a microfluidic separation column, an optical detection region substantially free of stationary phase material and disposed downstream of the column, and a porous membrane disposed downstream of the detection region. As noted by the Examiner, Ericson fails to disclose a porous membrane disposed downstream of an optical detection region. Office Action, pg. 3. Koehler discloses a porous frit used exclusively to retain stationary phase material within a separation column, but fails to even *mention* an optical detection region – let alone a *porous membrane disposed downstream* of such a region. Note that independent claim 1 requires that the optical detection region be “substantially free of stationary phase material.” As a result, it is doubly clear that the detection region cannot be part of a stationary-phase-containing separation column. Neither Ericson nor Koehler, whether alone or in combination, contain any disclosure of a porous membrane disposed downstream of an optical detection region that itself is disposed downstream of a separation column. Since Ericson and Koehler fail to teach all of the limitations of claim 1, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03. Moreover, since dependent claims represent a subset of their intervening claims and inherently include all the limitations of the claim(s) incorporated by reference into the dependent claim (37 CFR 1.75(c)), it is believed that dependent claims 3 and 6-12 should also be allowable as subsets of patentable claim 1. Accordingly, withdrawal of the rejections of these claims is respectfully requested.



3. Ericson And Koehler Fail To Teach All Of The Limitations Of Claims 21-23

Independent claim 21 requires, *inter alia*, “an optical detection region disposed ... between [a] separation region and [an] impedance region ... wherein the impedance region includes ... a substantially planar porous membrane.” As noted previously, Ericson fails to disclose a porous membrane disposed downstream of an optical detection region (Office Action, pg. 3), while Koehler discloses a porous frit used exclusively to retain stationary phase material within a separation column and makes no mention whatsoever of an optical detection region. Neither Ericson nor Koehler disclose a porous membrane disclosed downstream of an optical detection region, let alone the desirability of elevating the backpressure within such a detection region. Since Ericson and Koehler fail to teach all of the limitations of claim 21, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03. Moreover, pursuant to 37 CFR 1.75(c), it is believed that dependent claims 22 and 23 should also be allowable as subsets of patentable claim 21. Accordingly, withdrawal of the rejections of these claims is respectfully requested.

4. Ericson And Koehler Fail To Teach All Of The Limitations Of Claims 27-33

Independent claim 27 requires, *inter alia*, “a plurality of optical detection regions ... being disposed downstream of ... [a] plurality of [microfluidic] separation columns [and] being substantially free of stationary phase material ... and at least one porous material disposed downstream of the plurality of optical detection regions ... .” Ericson fails to disclose any porous material disposed downstream of an optical detection region substantially free of stationary phase material. See Ericson, pg. 82, Figure 2 & pg. 84, col. 1. While Koehler discloses a porous frit used exclusively to retain stationary phase material within a separation column, Koehler makes no mention whatsoever of an optical detection region – let alone an optical detection region disposed upstream of a porous material.

Since Ericson and Koehler fail to teach all of the limitations of claim 27, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03. Moreover, pursuant to 37 CFR 1.75(c), it is believed that dependent claims 28-33 should also be allowable as subsets of patentable claim 27. Accordingly, withdrawal of the rejections of these claims is respectfully requested.

H. Claims 13-20, 24-26, and 34 Are Patentable Over Ericson, Koehler, and Soga

Claims 13-20, 24-26, and 34 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Ericson in view of Koehler (Office Action, pg. 3.) Applicants respectfully traverse these rejections.

1. There Exists No Motivation To Combine Ericson, Koehler, and Soga To Yield The Combinations of Claims 13-20, 24-26, and 34

MPEP § 2143.01 requires the existence of a motivation to modify the reference or combine the teachings of multiple references to produce the claimed invention. Any teaching or suggestion to combine references must be found in the prior art. MPEP § 2143. As noted previously, there exists no motivation to combine Ericson and Koehler. Motivation is similarly lacking to add Soga to any such combination .

In the background of the invention, Soga specifically discusses **problems** associated with using **frits** and **particulate separation media** (Soga, Fig. 1 & ¶ 0005), similar to the teachings of Ericson (Ericson, col. 2). In contrast, Koehler is directed to the fabrication of multi-column chromatography devices specifically **having** a porous retaining frit disposed between particulate-containing separation columns and exit channels. Koehler, Fig. 3C; col. 7, lines 10-46; col. 10, lines 31-55. While Soga does disclose

detection regions 6, 6" (Soga, ¶ 0039), none of Ericson, Koehler, or Soga mention the desirability of elevating the backpressure within a detection region – let alone a *porous membrane or porous material disposed downstream of a detection region*. Since none of the references discloses the desirability for making the claimed combination, and both Ericson and Soga specifically **teach away** from the central disclosure of Koehler, one skilled in the art would **not** look to combine the two references to arrive at the claimed combinations. Under these facts, the Examiner has made an impermissible combination of the three references. See MPEP 2145(X)(D)(2) (“[i]t is improper to combine references where the references teach away from their combination) (*citing In re Grasselli (supra)*), As a result, with Ericson, Koehler, and Soga lacking any teaching or suggestion to combine references to produce the claimed invention, there can be no *prima facie* case of obviousness pursuant to MPEP § 2143.01, and it is respectfully requested that the § 103(a) rejections based on Ericson, Koehler, and Soga be withdrawn.

2. Ericson, Koehler, and Soga Fail To Teach All Of The Limitations Of Claims 13-20

Even if motivation existed to combine Ericson, Koehler, and Soga (which it does not), combining these references would not yield all of the limitations of independent claim 13. Claim 13 requires, *inter alia*, a “plurality of optical detection regions ... disposed downstream of ... [a] plurality of separation columns ... and at least one porous membrane disposed downstream of the plurality of optical detection regions ... .” As noted previously, neither Ericson nor Koehler disclose a porous membrane disposed downstream of an optical detection region that itself is disposed downstream of a separation column. While Soga does disclose detection regions (6, 6”), such regions are “formed inside the analysis channels 3, 3’ – **not downstream of** the analysis channels

(Soga, ¶ 0039 (emphasis added)), and Soga fails to teach or suggest the use of porous membranes. Claim 13 additionally requires that each optical detection region be “substantially free of stationary phase material.” Notably, the analysis channels 3, 3’ of Soga, which contain the detection regions 6, 6’, contain hardened silica gel (i.e., that serves as separation media). Soga, ¶¶ 0010, 0039-0040, 0044-0046. As a result, the detection regions 6, 6’ of Soga are not “substantially free of stationary phase material” as further required by claim 13. Since Ericson, Koehler, and Soga fail to teach all of the limitations of claim 13, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03. Moreover, since dependent claims represent a subset of their intervening claims and inherently include all the limitations of the claim(s) incorporated by reference into the dependent claim (37 CFR 1.75(c)), it is believed that dependent claims 14-20 should also be allowable as subsets of patentable claim 13. Accordingly, withdrawal of the rejections of these claims is respectfully requested.

3. Ericson, Koehler, and Soga Fail To Teach All Of The Limitations Of Claims 24-26

Even if motivation existed to combine Ericson, Koehler, and Soga (which it does not), combining these references would not yield all of the limitations of independent claim 24. Claim 24 requires, *inter alia*, “a plurality of optical detection regions disposed downstream of [a] plurality of separation columns ... and at least one porous membrane disposed downstream of the plurality of optical detection regions ... .” As discussed previously, none of Ericson, Koehler, or Soga disclose the use of a porous membrane disposed downstream of a plurality of optical detection regions. Since Ericson, Koehler, and Soga fail to teach all of the limitations of claim 24, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03. Moreover, since dependent claims represent a subset of their intervening claims and inherently include all the limitations of

the claim(s) incorporated by reference into the dependent claim (37 CFR 1.75(c)), it is believed that dependent claims 25-26 should also be allowable as subsets of patentable claim 24. Accordingly, withdrawal of the rejections of these claims is respectfully requested.

4. *Ericson, Koehler, and Soga Fail To Teach All Of The Limitations Of Claim 34*

Even if motivation existed to combine Ericson, Koehler, and Soga (which it does not), combining these references would not yield all of the limitations of claim 34. By virtue of its dependence on claim 27, claim 34 requires, *inter alia*, “a plurality of optical detection regions ... being disposed downstream of [a] plurality of separation columns [and] being substantially free of stationary phase material ... and at least one porous material disposed downstream of the plurality of optical detection regions ... .” While Ericson and Soga disclose optical detection regions and Koehler discloses a porous frit for retaining stationary phase material within a separation column, none of Ericson, Koehler, or Soga disclose the use of a porous material disposed downstream of a plurality of optical detection regions that are substantially free of stationary phase material. Since Ericson, Koehler, and Soga fail to teach all of the limitations of claim 34, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03, and withdrawal of the rejection of this claim is respectfully requested.

I. *Claims 27-30 and 32-34 Are Patentable Over Ericson, Shimada, and Hu*

Claims 27-30 and 32-34 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Ericson in view of Koehler (Office Action, pg. 3.) Applicants respectfully traverse these rejections.

1. *There Exists No Motivation To Combine Ericson, Shimada, and Hu To Yield The Combinations of Claims 27-30 and 32-34*

MPEP § 2143.01 requires the existence of a motivation to modify the reference or combine the teachings of multiple references to produce the claimed invention. Any teaching or suggestion to combine references must be found in the prior art. MPEP § 2143. Contrary to the Examiner's assertion, it would not have been obvious to combine Ericson, Shimada, and Hu to arrive at any of claims 27-30 and 32-34. Shimada discloses a chromatography system utilizing a single column that is packed with particulate material. Shimada, col. 1, lines 16-19; col. 2, lines 49-50. In sharp contrast to Shimada, Ericson discloses the use of a continuous polymer bed in a microchip or capillary tube to specifically **avoid** the use of a supporting frit to retain a bed of packed beads. Ericson, col. 2. Hu fails to bridge the gap in that it discloses the use of gel separation media for performing electrically driven separations (e.g., capillary electrophoresis or isoelectric focusing). Hu, col. 2, lines 56-59; col. 6, lines 34-39; col. 11, line 66 – col. 12, line 30; col. 13, line 58 – col. 14, line 11; col. 15, lines 9-15; col. 15, lines 55-58; col. 16, lines 29-42. Additionally, claims 27-30 and 32-34 require “a plurality of separation columns” – something from which Shimada specifically **teaches away**. See Shimada, col. 1, lines 35-54. With the contradictory teachings of Shimada and Ericson, one skilled in the art would not look to combine the references to arrive at claims 27-30 and 32-34. Moreover, the Examiner has made an impermissible combination of the two references pursuant to MPEP 2145(X)(D)(2) and In re Grasselli (*supra*). As a result, with Shimada and Ericson lacking any teaching or suggestion to combine references to produce the claimed invention, there can be no *prima facie* case of obviousness pursuant to MPEP § 2143.01, and it is respectfully requested that the § 103(a) rejections based on Shimada, Ericson, and Hu be withdrawn.

2. *Ericson, Shimada, Hu Fail To Teach All Of The Limitations Of Claims 27-30 and 32-34*

Even if motivation existed to combine Ericson, Koehler, and Soga (which it does not), combining these references would not yield all of the limitations of independent claim 27. Claim 27 requires, *inter alia*, “a **plurality of microfluidic separation columns** ... containing packed particulate stationary phase material retained by a frit ... .” Ericson discloses the use of a continuous polymer bed in a microchip or capillary to specifically avoid the use of porous frits to retain packed beads. Ericson, pg. 81, cols. 1-2. In contrast, Shimada teaches the use of a conventional-scale column having packed particulate material. Shimada, col. 1, lines 16-19; col. 2, lines 49-50. Shimada further teaches away from the use of multi-column chromatography systems (e.g., to avoid measurement errors, reduce eluent consumption, and avoid complicated structure). Shimada, col. 1, lines 35-54. Hu discloses gel-filled channels for electrically-driven separation processes. Hu, col. 2, lines 56-59; col. 6, lines 34-39; col. 11, line 66 – col. 12, line 30; col. 13, line 58 – col. 14, line 11; col. 15, lines 9-15; col. 15, lines 55-58; col. 16, lines 29-42. Any combination of Ericson, Shimada, and Hu would not yield multiple separation columns containing packed particulate stationary phase material retained by a frit. Since Ericson, Shimada, and Hu fail to teach all of the limitations of claim 27, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03. Moreover, since dependent claims represent a subset of their intervening claims and inherently include all the limitations of the claim(s) incorporated by reference into the dependent claim (37 CFR 1.75(c)), it is believed that dependent claims 28-30 and 32-34 should also be allowable as subsets of patentable claim 27. Accordingly, withdrawal of the rejections of these claims is respectfully requested.

## II. Claim Rejections Under The Judicially Created Doctrine of Obviousness-Type Double Patenting

### A. Law Regarding Obviousness-Type Double Patenting

A rejection based on nonstatutory double patenting is based on a judicially created doctrine grounded in public policy so as to prevent the unjustified or improper timewise extension of the right to exclude granted by a patent. MPEP 804(II)(B) (citations omitted). “[D]ouble patenting is not ‘concerned with what one skilled in the art would be *aware [of]* from reading the claims but with what *inventions* the claims define.’” Eli Lilly & Co. v. Barr Labs., 55 USPQ2d 1609, 1618 (Fed. Cir. 2000) (emphasis added), *quoting In re Sarett*, 51 C.C.P.A. 1180, 327 F.2d 1005, 1013, 140 USPQ 474, 481 (C.C.P.A. 1964). As stated in MPEP 804(II)(B)(1):

A double patenting rejection of the obviousness-type is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. In re Braithwaite, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, any analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. In re Braat, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Moreover, “[a]ny obviousness-type double patenting rejection should make clear:

- (A) The differences between the inventions defined by the conflicting claims - a claim in the patent compared to a claim in the application; and
- (B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in a claim in the patent.

MPEP 804(II)(B)(1). “When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art.” Id.



The Federal Circuit has held that the Examiner's showing of obviousness must follow the analysis used to establish a *prima facie* case of obviousness. See In re Longi, 759 F.2d 887, 225 USPQ 645, 651 (Fed. Cir. 1985) (Examiner must provide *prima facie* case of obviousness for obviousness-type double patenting rejection; burden then shifts to applicant to rebut *prima facie* case.) The differences between a double patenting rejection and a rejection based on prior art are identified in the MPEP:

One significant difference is that a double patenting rejection must rely on a comparison with the claims in an issued or to be issued patent, whereas an obviousness rejection based on the same patent under 35 U.S.C. 102(e)/103(a) relies on a comparison with what is disclosed (whether or not claimed) in the same issued or to be issued patent. In a 35 U.S.C. 102(e)/103(a) rejection over a prior art patent, the reference patent is available for all that it fairly discloses to one of ordinary skill in the art, regardless of what is claimed. In re Bowers, 359 F.2d 886, 149 USPQ 570 (CCPA 1966).

MPEP 804(III).

B. Claims 1, 3, 6-12, 21-23, and 27-33 Are Patentable Over Claims 1, 21, 31, and 32 of U.S. Serial No. 10/313,231 (Now U.S. Patent No. 6,848,462), Claims 1, 4, and 10 of U.S. 6,814,859, and Ericson

Claims 1, 3, 6-12, 21-23, and 27-33 were rejected under the judicially-created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1, 21, 31, and 32 of U.S. application Serial No. 10/313,231 in view of claims 1, 4, and 10 of U.S. Patent No. 6,814,859 and in view of Ericson. Office Action, pgs. 6-7. After the Office Action was mailed, U.S. Patent No. 6,848,462 issued on application Serial No. 10/313,231, thus eliminating the "provisional" status of the Examiner's obviousness-type double patenting rejection. Applicants respectfully traverse this rejection for the reasons provided below.

1. *Inventions Defined By Claims 1, 21, 31, and 32 of U.S. Serial No. 10/313,231 (now U.S. Patent No. 6,848,462)*

Claims 1 and 21 of U.S. Patent No. 6,848,462 are directed generally to adhesiveless methods for fabricating microfluidic devices from cover layers and at least one stencil layer between controllably heated platens, as provided in more detail below:

1. A method for fabricating a microfluidic device, the method comprising the steps of:
  - providing a first substantially flat platen and a second substantially flat platen;
  - providing a plurality of substantially planar, substantially metal-free, adhesiveless polymer device layers including:
    - a first cover layer and a second cover layer, at least one of the first cover layer and the second cover layer defining a fluidic port; and
    - at least one stencil layer defining a microfluidic channel penetrating through the entire thickness of the at least one stencil layer, the microfluidic channel being bounded laterally by the at least one stencil layer, and being bounded from above and below by additional device layers of the plurality of device layers to define an upper channel surface and a lower channel surface;
  - stacking the plurality of device layers between the first platen and the second platen; and
  - controllably heating the plurality of stacked device layers according to a heating profile adapted to form a substantially sealed adhesiveless microfluidic device wherein the upper channel surface remains distinct from the lower channel surface.

21. The method of claim 1 wherein the polymer comprises a polyolefin material.

Similarly, claims 31 and 32 of U.S. Patent No. 6,848,462 are directed generally to adhesiveless polymeric microfluidic devices including a first cover layer, a second cover layer, and at least one intermediate stencil layer disposed therebetween, with the layers being interpenetrably bound together to form a substantially sealed device, as described in more detail below:

31. An adhesiveless microfluidic device comprising a plurality of substantially planar device layers including:
- a first cover layer and a second cover layer, with at least one cover layer defining a fluidic port; and
  - at least one stencil layer disposed between the first cover layer and the second cover layer, the at least one stencil defining a microfluidic channel through the entire thickness of the at least one stencil layer, the channel being bounded from above and below by additional device layers of the plurality of device layers to define an upper channel surface and a lower channel surface, and the channel being in fluid communication with the fluidic port;
- wherein the first cover layer, second cover layer, and the at least one stencil layer are fabricated with substantially metal-free, adhesiveless polymer materials, and the layers are interpenetrably bound together to form a substantially sealed adhesiveless microstructure with the upper surface remaining distinct from the lower surface.

32. The device of claim 31 wherein the resulting microfluidic device remains substantially sealed with an internal fluid pressure of at least about 100 psi.

2. *Inventions Defined By Claims 1, 4, and 10 of U.S. Patent No. 6,814,859*

Claims 1, 4, and 10 of U.S. Patent No. 6,814,859 (or "Koehler" as described previously herein) are directed generally to stencil-based microfluidic separation devices having multiple separation columns and a (liquid permeable) single frit spanning multiple flow paths within the devices, as described in more detail below:

1. A multi-layer microfluidic separation device comprising:
- a first stencil layer defining the lateral boundaries of a plurality of separation columns;
  - a second stencil layer defining the lateral boundaries of a plurality of exit channels wherein the plurality of exit channels is in fluid communication with the plurality of separation channels to form a plurality of fluid flow paths; and
  - a single frit having an upper surface and a lower surface, wherein the upper surface is bonded to the first stencil layer and the lower surface is bonded to the second stencil layer such that the frit layer is disposed within at least two fluid flow paths of the plurality of fluid flow paths;
- wherein the frit permits flow in a direction substantially perpendicular to the upper surface and the lower surface;

wherein the upper surface is sufficiently bonded to the first stencil layer and the lower surface is sufficiently bonded to the second stencil layer to prevent substantially any lateral flow of fluid at an operating pressure either between the first stencil layer and the frit or between the second stencil layer and the frit.

4. The multi-layer microfluidic separation device of claim 1 wherein the operating pressure is at least about 100 psi (690 kPa).

10. The multi-layer microfluidic separation device of claim 1 wherein the frit comprises a permeable polypropylene membrane.

3. Disclosure of Ericson (Anal. Chem. 2000, Vol. 72, pp. 81-87)

Ericson discloses the fabrication and use of microchips and capillary tubes having continuous polymer beds (serving as stationary phase material) for performing chromatography. Ericson, pg. 81, cols. 1-2. (Such beds are referred to elsewhere as monolithic columns.) The disclosed benefits of using a continuous packed bed are: (1) eliminating "wall effects" by anchoring the beds to the wall of surrounding channel; and (2) **eliminating** the use of **porous frits to retain packed beads** of stationary phase material, recognizing that "the difficulty of affixing frits to support the bed [of packed beads] is obvious." Id. Restating the point, Ericson provides that with a "continuous bed ... anchored to the channel wall ... [n]o supporting frit is, therefore, required." Id. at col. 2.

To fabricate microchips, Ericson teaches the use of photolithographic etching to define channels a quartz substrate. Ericson, pg. 82, cols. 1-2. The quartz chip was mounted on a supporting plate of black Plexiglass with a slit for UV detection. Id., pg. 83, col. 1. Two different microchip designs were employed: one having a serpentine column, and the other purportedly having an "h"-shaped column. Id. at pg. 82, Fig. 2 &

caption relating to “C” and “D”. Following device fabrication, the channel walls were chemically activated with methacrylol groups to facilitate covalent bonding of polymer bed material. *Id.* at pg. 83, col. 2. Thereafter, various types of continuous polymer beds (i.e., monolithic columns) were prepared directly in the channels of the microchips by polymerizing monomer solutions in situ. *Id.* at pg 83, col. 2 – pg. 84, col. 1. A poly(ethylene glycol) solution was used in the outlet channel to create a sharper and more homogenous end of the polymer bed. *Id.* at pg. 83, col. 2 – pg. 84, col. 1. UV detection may be performed through the slit in the (Plexiglas) supporting plate at a spot close to (downstream) of the polymer bed. *Id.* at pg. 84, col. 1. Ericson also discloses that detection could also be done directly through the somewhat UV-transmitting continuous bed, but such detection would be far less preferable due to a tenfold reduction in sensitivity. *Id.*

Ericson fails to mention the desirability of elevating the backpressure within a detection region, let alone any structure capable of accomplishing such a purpose.

4. *There Exists No Motivation To Combine Ericson With Claims 1, 4, and 10 of U.S. Patent No. 6,814,859 (to Koehler)*

To support a prima facie case of obviousness, MPEP § 2143.01 requires the existence of a motivation to modify the reference or combine the teachings of multiple references to produce the claimed invention. Any teaching or suggestion to combine references must be found in the prior art. MPEP § 2143. Contrary to the Examiner’s assertion (Office Action, pp. 6-7), it would **not** have been obvious to combine Ericson with claims 1, 4, and 10 of U.S. Patent No. 6,814,959 to Koehler. Ericson discloses the use of a continuous polymer bed in a microchip or capillary to specifically **avoid** the use of a supporting frit to retain a bed of packed beads. Ericson, col. 2. In sharp contrast to

Ericson, claims 1, 4, and 10 of U.S. 6,814,859 **require** a frit disposed within at least two fluid flow paths communicating with a plurality of separation columns. Additionally, presently pending claims 1, 3, 6-12, 21-23, and 27-33 all require either a porous membrane or porous material disposed downstream of (at least one) optical detection region. There exists no teaching in Ericson, in claims 1, 4, and 10 of U.S. 6,814,959, or in claims 1, 21, 31, and 32 of U.S. 6,848,462 to produce such a structure. Since none of Ericson or the cited claims (i.e., of U.S. 6,814,959 and U.S. 6,848,462) discloses the desirability for making the claimed combination, and Ericson specifically **teaches away** from claims 1, 4, and 10 of U.S. 6,814,859 (incorporating frits into microfluidic devices), one skilled in the art would **not** look to combine these references to arrive at presently claimed 1, 3, 6-12, 21-23, and 27-33. Under these facts, the Examiner has made an impermissible combination of the references. See MPEP 2145(X)(D)(2) (“[i]t is improper to combine references where the references teach away from their combination) (*citing In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983)). As a result, there can be no *prima facie* case of obviousness pursuant to MPEP § 2143.01, such as would be required under *In re Longi*, 759 F.2d 887, 225 USPQ 645, 651 (Fed. Cir. 1985) to support a rejection based on obviousness-type double patenting, and it is respectfully requested that the obviousness-type double patenting rejections of claims 1, 3, 6-12, 21-23, and 27-33 be withdrawn.

5. Ericson, Claims 1, 21, 31, and 32 of U.S. 6,814,859, and Claims 1, 4, and 10 of U.S. 6,814,859 Fail To Teach All The Limitations of Claims 1, 3, and 6-12

Even if there existed motivation to combine Ericson, claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S. 6,814,859 (which there does not), presently pending independent claim 1 requires, *inter alia*, a microfluidic separation

column, an optical detection region substantially free of stationary phase material and disposed downstream of the column, and a porous membrane disposed downstream of the detection region. As noted by the Examiner, Ericson fails to disclose a porous membrane disposed downstream of an optical detection region. Office Action, pg. 3. None of claims 1, 21, 31, and 32 of U.S. 6,814,859 or claims 1, 4, and 10 of U.S. 6,814,859 disclose a porous membrane disposed downstream of an optical detection region either. Since Ericson, claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S. 6,814,859 fail to teach all of the limitations of claim 1, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03 (as would be required under In re Longi, 759 F.2d 887, 225 USPQ 645, 651 (Fed. Cir. 1985) to support a rejection based on obviousness-type double patenting. Moreover, since dependent claims represent a subset of their intervening claims and inherently include all the limitations of the claim(s) incorporated by reference into the dependent claim (37 CFR 1.75(c)), it is believed that dependent claims 3 and 6-12 should also be allowable as subsets of patentable claim 1. Accordingly, withdrawal of the rejections of these claims is respectfully requested.

6. Ericson, Claims 1, 21, 31, and 32 of U.S. 6,814,859, and Claims 1, 4, and 10 of U.S. 6,814,859 Fail To Teach All The Limitations of Claims 21-23

Claim 21 requires, *inter alia*, “an optical detection region disposed ... between [a] separation region and [an] impedance region ... wherein the impedance region includes ... a substantially planar porous membrane.” As noted previously, Ericson fails to disclose a porous membrane disposed downstream of an optical detection region (Office Action, pg. 3). None of claims 1, 21, 31, and 32 of U.S. 6,814,859 or claims 1, 4, and 10 of U.S. 6,814,859 disclose such a combination either. Since Ericson, claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S. 6,814,859 fail to teach all of the

limitations of claim 21, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03 (as would be required under In re Longi, 759 F.2d 887, 225 USPQ 645, 651 (Fed. Cir. 1985) to support a rejection based on obviousness-type double patenting. Moreover, since dependent claims represent a subset of their intervening claims and inherently include all the limitations of the claim(s) incorporated by reference into the dependent claim (37 CFR 1.75(c)), it is believed that dependent claims 22-23 should also be allowable as subsets of patentable claim 21. Accordingly, withdrawal of the rejections of these claims is respectfully requested.

7. *Ericson, Claims 1, 21, 31, and 32 of U.S. 6,814,859, and Claims 1, 4, and 10 of U.S. 6,814,859 Fail To Teach All The Limitations of Claims 27-33*

Independent claim 27 requires, *inter alia*, “a plurality of optical detection regions ... being disposed downstream of ... [a] plurality of [microfluidic] separation columns [and] being substantially free of stationary phase material ... and at least one porous material disposed downstream of the plurality of optical detection regions ... .” Ericson fails to disclose any porous material disposed downstream of an optical detection region substantially free of stationary phase material. See Ericson, pg. 82, Figure 2 & pg. 84, col. 1. None of claims 1, 21, 31, and 32 of U.S. 6,814,859 or claims 1, 4, and 10 of U.S. 6,814,859 disclose such a combination either. Since Ericson, claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S. 6,814,859 fail to teach all of the limitations of claim 27, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03 (as would be required under In re Longi, 759 F.2d 887, 225 USPQ 645, 651 (Fed. Cir. 1985) to support a rejection based on obviousness-type double patenting. Moreover, since dependent claims represent a subset of their intervening claims and inherently include all the limitations of the claim(s) incorporated by reference



into the dependent claim (37 CFR 1.75(c)), it is believed that dependent claims 28-33 should also be allowable as subsets of patentable claim 27. Accordingly, withdrawal of the rejections of these claims is respectfully requested.

C. Claims 13-20, 24-26, and 34 Are Patentable Over Claims 1, 21, 31, and 32 of U.S. Serial No. 10/313,231 (Now U.S. Patent No. 6,848,462), Claims 1, 4, and 10 of U.S. 6,814,859, Ericson, and Soga

Claims 13-20, 24-26, and 34 were rejected under the judicially-created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1, 21, 31, and 32 of U.S. application Serial No. 10/313,231 in view of claims 1, 4, and 10 of U.S. Patent No. 6,814,859, in view of Ericson, and in view of Soga. Office Action, pg. 8. The inventions defined by claims 1, 21, 31, and 32 of U.S. 6,848,462 and by claims 1, 4, and 10 of U.S. 6,814,859 are described above, such as were described the disclosures of Ericson and Soga. After the Office Action was mailed, U.S. Patent No. 6,848,462 issued on application Serial No. 10/313,231, thus eliminating the “provisional” status of the Examiner’s obviousness-type double patenting rejection. Applicants respectfully traverse this rejection for the reasons provided below.

1. There Exists No Motivation To Combine Ericson or Soga With Claims 1, 4, and 10 of U.S. Patent No. 6,814,859 (Koehler)

To support a prima facie case of obviousness, MPEP § 2143.01 requires the existence of a motivation to modify the reference or combine the teachings of multiple references to produce the claimed invention. Any teaching or suggestion to combine references must be found in the prior art. MPEP § 2143. Contrary to the Examiner’s assertion (Office Action, pp. 8), it would **not** have been obvious to combine either Soga or Ericson with claims 1, 4, and 10 of U.S. Patent No. 6,814,959 to Koehler. Ericson

discloses the use of a continuous polymer bed in a microchip or capillary to specifically **avoid** the use of a supporting frit to retain a bed of packed beads. Ericson, col. 2.

Similarly, Soga specifically discusses **problems** associated with using **frits** and filling channels with **microparticle separation media** (Soga, ¶¶ 0005, 0007) and teaches the synthesis of unified monolithic porous bodies as separation media (Soga, ¶¶ 0007, 0010, 0039-0040, 0044-0046). In sharp contrast to Ericson, claims 1, 4, and 10 of U.S.

6,814,859 **require a frit** disposed within at least two fluid flow paths communicating with a plurality of separation columns. Additionally, presently pending claims 13-20, 24-26, and 34 all require either a porous membrane or porous material disposed downstream of

(at least one) optical detection region. There exists no teaching in Ericson, in Soga, in claims 1, 4, and 10 of U.S. 6,814,959, or in claims 1, 21, 31, and 32 of U.S. 6,848,462 to produce such a structure. Since none of Ericson, Soga, or the cited claims (i.e., of U.S. 6,814,959 and U.S. 6,848,462) discloses the desirability for making the claimed

combination, and since Ericson and Soga specifically **teaches away** from claims 1, 4, and 10 of U.S. 6,814,859 (incorporating frits into microfluidic devices), one skilled in the art would **not** look to combine these references to arrive at presently claimed 13-20, 24-26, and 34. Under these facts, the Examiner has made an impermissible combination of

the references. See MPEP 2145(X)(D)(2) (“[i]t is improper to combine references where the references teach away from their combination”) (*citing In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983)). As a result, there can be no *prima facie*

case of obviousness pursuant to MPEP § 2143.01, such as would be required under In re Longi, 759 F.2d 887, 225 USPQ 645, 651 (Fed. Cir. 1985) to support a rejection based

on obviousness-type double patenting, and it is respectfully requested that the obviousness-type double patenting rejections of claims 13-20, 24-26, and 34 be withdrawn.

2. *Ericson, Claims 1, 21, 31, and 32 of U.S. 6,814,859, and Claims 1, 4, and 10 of U.S. 6,814,859 Fail To Teach All The Limitations of Claims 13-20*

Even if there existed motivation to combine Ericson, Soga, claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S. 6,814,859 (which there does not), presently pending independent claim 13 requires, *inter alia*, a “plurality of optical detection regions ... disposed downstream of ... [a] plurality of separation columns ... and at least one porous membrane disposed downstream of the plurality of optical detection regions ... .” As noted previously, Ericson does not disclose a porous membrane disposed downstream of an optical detection region that itself is disposed downstream of a separation column. While Soga does disclose detection regions (6, 6’), such regions are “formed inside the analysis channels 3, 3’ – not downstream of the analysis channels (Soga, ¶ 0039 (emphasis added)), and Soga fails to teach or suggest the use of porous membranes. Claim 13 additionally requires that each optical detection region be “substantially free of stationary phase material.” Notably, the analysis channels 3, 3’ of Soga, which contain the detection regions 6, 6’, contain hardened silica gel (i.e., that serves as separation media). Soga, ¶¶ 0010, 0039-0040, 0044-0046. As a result, the detection regions 6, 6’ of Soga are not “substantially free of stationary phase material” as further required by claim 13. None of claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S. 6,814,859 disclose a porous membrane disposed downstream of an optical detection region that itself is disposed downstream of a separation column. Since Ericson, Soga, claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S. 6,814,859 fail to teach all of the limitations of claim 13, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03 (as would be required

under In re Longi, 759 F.2d 887, 225 USPQ 645, 651 (Fed. Cir. 1985) to support a rejection based on obviousness-type double patenting. Moreover, since dependent claims represent a subset of their intervening claims and inherently include all the limitations of the claim(s) incorporated by reference into the dependent claim (37 CFR 1.75(c)), it is believed that dependent claims 14-20 should also be allowable as subsets of patentable claim 13. Accordingly, withdrawal of the rejections of these claims is respectfully requested.

3. *Ericson, Claims 1, 21, 31, and 32 of U.S. 6,814,859, and Claims 1, 4, and 10 of U.S. 6,814,859 Fail To Teach All The Limitations of Claims 24-26*

Independent claim 24 requires, *inter alia*, “a plurality of optical detection regions disposed downstream of [a] plurality of separation columns ... and at least one porous membrane disposed downstream of the plurality of optical detection regions ... .”

Neither Ericson nor Soga disclose a porous membrane disposed downstream of an optical detection region that itself is disposed downstream of a separation column.

While Soga does disclose detection regions (6, 6”), such regions are “formed inside the analysis channels 3, 3’ – not downstream of the analysis channels (Soga, ¶ 0039 (emphasis added)), and Soga fails to teach or suggest the use of porous membranes.

None of claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S.

6,814,859 disclose a porous membrane disposed downstream of an optical detection region that itself is disposed downstream of a separation column. Since Ericson, Soga, claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S. 6,814,859 fail to teach all of the limitations of claim 24, they cannot support a *prima facie* case of

obviousness pursuant to M.P.E.P. § 2143.03 (as would be required under In re Longi, 759 F.2d 887, 225 USPQ 645, 651 (Fed. Cir. 1985) to support a rejection based on

obviousness-type double patenting. Moreover, since dependent claims represent a subset of their intervening claims and inherently include all the limitations of the claim(s) incorporated by reference into the dependent claim (37 CFR 1.75(c)), it is believed that dependent claims 25-26 should also be allowable as subsets of patentable claim 24. Accordingly, withdrawal of the rejections of these claims is respectfully requested.

4. *Ericson, Claims 1, 21, 31, and 32 of U.S. 6,814,859, and Claims 1, 4, and 10 of U.S. 6,814,859 Fail To Teach All The Limitations of Claims 34*

Even if motivation existed to combine Ericson, Soga, claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S. 6,814,859 (which it does not), combining these references would not yield all of the limitations of claim 34. By virtue of its dependence on claim 27, claim 34 requires, *inter alia*, “a plurality of optical detection regions ... being disposed downstream of [a] plurality of separation columns [and] being substantially free of stationary phase material ... and at least one porous material disposed downstream of the plurality of optical detection regions ... .” None of Ericson, Soga, claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S. 6,814,859 disclose the use of a porous material disposed downstream of a plurality of optical detection regions that are substantially free of stationary phase material. Since Ericson, Soga, claims 1, 21, 31, and 32 of U.S. 6,814,859, and claims 1, 4, and 10 of U.S. 6,814,859 fail to teach all of the limitations of claim 24, they cannot support a *prima facie* case of obviousness pursuant to M.P.E.P. § 2143.03 (as would be required under In re Longi, 759 F.2d 887, 225 USPQ 645, 651 (Fed. Cir. 1985) to support a rejection based on obviousness-type double patenting, and withdrawal of the rejection of claim 34 in this regard is respectfully requested.

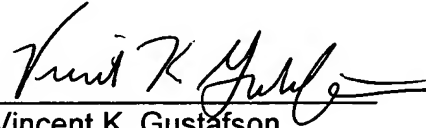
**Conclusion**

By virtue of the amendments and arguments provided herein, Applicants believe that all pending claims 1, 3, and 6-34 are in good condition for allowance, and respectfully request allowance thereof. Consideration of the enclosed Information Disclosure Statement is also requested.

If any additional information should be required in considering this Response, or if there are any questions or deficiencies with regard to this Response that can be addressed by telephone, the USPTO representative is encouraged to contact the undersigned directly at (626) 351-8200, ext. 6503.

Respectfully submitted,

Dated: February 18, 2005

  
Vincent K. Gustafson  
Reg. No. 46,182

**USPTO Customer No.: 32763**

Encl: Information Disclosure Statement with completed Form PTO-1449 and one copy each of cited (non-US patent) references